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AN APPARATUS FOR DETERMINING THE POSITION OF AN OBJECT

FIELD OF THE INVENTION

The present invention relates to a method and an apparatus that provides rapid scanning of large specimens to detect and determine positions of objects having specific characteristics. The apparatus may, further, be adapted to store information associated with the positions of the objects and also adapted to identify the objects. The positions of the objects and/or their identities may be stored in a volatile or a non-volatile memory location. The specimen may be provided for scanning on a solid support, such as a circular disc. The objects may be cells or microorganisms of a particular rare type i.e. they may have a very low density in the specimen.

BACKGROUND OF THE INVENTION

In US 5,374,989 an apparatus for identifying an object having a non-specific outer boundary is disclosed. The apparatus comprises a tracking device for tracking a position of the object to be identified in two dimensions and an identification device for identification of the tracked object. The objects to be identified may be stained so as to distinguish them from other objects by a difference in transmissivity at a specific range of wavelengths. The object identification device comprises a coherent light source illuminating an area of the specimen and a detection device with a plurality of circular coaxial sections which are detecting the intensity distribution of a Fourier transform of light transmitted through the objects of the specimen.

US 5,663,057 discloses an apparatus and a process for rapid counting of fluorescent microorganisms in a specimen. A solid support, such as a filter, holding the fluorescent microorganisms is scanned line by line with a laser beam having a circular focus area, with a diameter between 4 and 14 µm, on the filter. The emitted fluorescence is measured at one or more predetermined wavelengths. The scanning lines on the filter are produced in an overlapping pattern, and line-to line features are compared in time synchrony to eliminate uncorrelated events like random noise etc. A digital signal processing circuit applies a set of predetermined mathematical algorithms to the obtained fluorescent light signals to avoid or minimise detection of false positive responses and false negative responses.

The above mentioned types of prior art apparatuses utilises a Cartesian (x,y) scanning and tracking methodology, whereby the specimen is scanned line by line and the particular type of objects are recognised by either detecting emitted light from the objects or by detecting characteristic parameters of an optical Fourier transformation of light transmitted through the objects.

These prior art methods of identification and location of the objects are slow when the particular type of objects or target objects are very rare in the specimen, i.e. they may have a density of 1E-6 or less. This is due to the Cartesian scanning of the specimen and the small focus area of the laser beam combined with the large number of objects, which have to be analysed before it is likely that a target object is located and identified. Further, due to the limited dimensions of the specimen

provided by these prior art methods, it may not contain any target objects at all.

SUMMARY OF THE INVENTION

Accordingly, it is an object of the present invention to provide a method and apparatus providing a rapid scan of a large area specimen and, simultaneously, detect target objects and determine their positions.

It is also an object of the present invention to provide an apparatus, which may store the positions of the detected target objects in a volatile or a non-volatile memory location. The positions of the detected target objects may subsequently be retrieved from the memory, and the objects may be subjected to a thorough analysis in order to establish their identity.

An apparatus according to the present invention may provide a solid support, adapted to receive and hold the specimen, with an area at least twenty times larger than the at most 400 mm^2, utilised in prior art apparatuses.

The apparatus may also be adapted to provide rapid scanning of specimens provided on slides of standard sizes such specimens are commonly used in microscopy in the medical field.

The large area of the specimen that may be scanned by the present apparatus is a significant advantage, especially in applications involving detection of very rare target objects, since a substantially larger number of target objects may be provided in the specimen in comparison

with the number of target objects provided by prior art apparatuses.

It is further an advantage of the present invention that it may utilise a light source capable of irradiating, on the specimen, a focus area substantially larger than focus areas provided by prior art apparatuses. The large focus area, which may be provided by an embodiment of an apparatus according to the invention, enables rapid scanning of even very large specimens.

Accordingly, an apparatus is provided for detecting a property of an object contained in a specimen, comprising a frame, a member positioned on the frame and having a surface that is adapted to receive and hold the specimen, a detector for detection of the property of the object, and scanning means for scanning the specimen in relation to the detector along a non-linear curve.

The member may, further, be positioned for rotation about an axis on the frame and the scanning means comprise means for rotating the member about the axis.

The apparatus may further comprise scanning control means for controlling the scanning means for scanning the specimen along a predetermined curve, such as a substantially circular curve.

The apparatus may further comprise storage means for storage of signals provided by the detector and corresponding position signals provided by the scanning control means, and also means for sampling and digitising the detector signals and the position signals

Signal processing means, may further be provided, connected to the detector and adapted to receive detector signals and detect presence of an object based on the detector signals. Position signals relating to detected objects may subsequently be stored in the storage means.

Preferably, the area of the specimen submitted for scanning is larger than 500 mm^2, even more preferably larger than 8000 mm^2.

In one embodiment of the invention, a particular property of the target objects in the specimen is provided by staining them with a magnetic marker. By scanning the specimen with a magnetic sensitive detector, such as a magnetic reading head, the target objects and their positions may be detected.

In another embodiment of the invention, the target objects may be stained with a fluorescent marker and a light source also provided that emits a first light beam towards the specimen. Further, a light sensitive detector may be provided in this apparatus for detection of light emitted from the target object or objects upon interaction with the first light beam during the scanning.

In embodiments of the apparatus wherein the light source is utilised, the scanning of the specimen may be performed by at least three different methods. Each of the scan methodologies may correspond to one particular embodiment of the invention, as detailed below.

In a first and preferred embodiment, the member is positioned on the frame of the apparatus. The light

source may emit the first light beam towards the specimen, which is provided on a disc and the scanning means may be adapted to scan the beam across the specimen along the non-linear curve. The detector detects light emitted from objects comprised in the specimen upon interaction with the first light beam during scanning of the specimen. The member may be positioned for rotation about an axis of the apparatus frame. The scanning means may comprise a DC motor and a spindle rigidly connected to the motor. The spindle may, further, be connected to the member which, preferably, is a substantially circular disc, holding the specimen so that the specimen may be rotated about the axis of the apparatus frame. The scanning means may also comprise deflecting means that may comprise a servo motor or a stepper motor connected to the member holding the specimen and thereby adapted to scan the first light beam along a radius of the circular movement of the disc holding the specimen.

According to another, second, embodiment of the invention, the member holding the specimen may be stationary relative to the apparatus frame during the scanning. Instead the light source may be positioned for rotation about the axis on the frame and the scanning means may comprise means, which are adapted to rotate the light source about the axis. The scanning means may, further, comprise deflecting means adapted to scan the first light beam across the specimen along a radius of the circular movement of the light source. This second embodiment is particularly advantageous if the specimen comprising the objects is provided in an unstable physical state, e.g. in a liquid nutritional solution that allows the target objects to multiply prior to the scanning. A liquid specimen may be scanned without

shifting positions of objects in the specimen, since they are not subjected to centripetal forces produced by rotation of the specimen.

According to a third and yet other embodiment of the invention, the light source emitting the first beam and the member holding the specimen may be stationary relative to the apparatus frame during the scanning. Instead moveable deflecting means, which may comprise a mirror, may be provided to rotate around a first axis, thereby enabling the first light beam to be scanned across the specimen along a substantially circular curve. The moveable mirror may further be rotatable around a second axis to vary the radius of the circular curve on the specimen, so that the specimen may be scanned by the light beam along an e.g. Archimedes´ spiral curve.

A non-linear curve is in the present context a curve, which can not be generated by any, finite, number of straight lines. Preferably, the non-linear curve is provided as an Archimedes´ spiral curve or a curve comprising a number of substantially concentric circular curves.

The target object or objects may be a particular type of biological cell(s), bacteria, micro-organisms, etc. as commonly of relevance in the medical field.

In the medical field, these target cells or target micro-organisms may be found in specimens, which also comprise a large number of resembling cells or micro-organisms. These resembling cells may constitute the main substance of the specimen, thereby being present in a much larger density than the density of the target cells.

The discrimination between the target object(s) and the objects of the main substance may be based on differences in morphological, magnetic, or optical characteristics.

The target objects are, preferably, stained by utilising antibody coupled magnetic beads or probes conjugated with fluorescent markers to provide the needed difference from the objects of the main substance, and thereby serve as basis for the discrimination. Both types of antibody probes with fluorescent markers are today commercially available.

The objects may further be provided in a solution and the solution may be deposited on a substantially circular disc that may constitute the solid support adapted to hold the specimen.

An initial enrichment of the solution comprising the objects may be provided before the specimen is submitted for scanning. This initial enrichment may comprise the step of sorting the target objects from the objects of the main substance and/or the step of letting the target objects multiply (through reproduction), thereby enlarging the density of target objects in the specimen prior to scanning.

When a disc is used as a solid support being adapted to hold the specimen, there exist, in principle, only few limitations to the disc size. Preferably, a disc diameter of approximately 120 mm, which is equal to the diameter of a CD, is utilised. This has several significant advantages, one advantage is that the effective area of a CD size disc is at least twenty times larger than the

typical solid support area used in prior art apparatuses. Another advantage is that suitable mechanical and optical parts for the present apparatus may be found readily available and at a very low cost due to the wide spread use of CD based media. The disc may be made of a transparent material, such as polycarbonate, glass, etc.

In a preferred embodiment, the detection of target objects is provided by scanning a first light beam across the specimen along a non-linear curve. This first light beam provides a light spot on the specimen, which irradiates the objects of the main substance together with any present target objects. The light beam may be provided by a monochromatic coherent light source, such as a semi-conductor laser, gas laser, solid state laser, etc.

Alternatively, the light source may be of a type that emits broad-banded light. An optical filter may be inserted in the optical path between the light source and the specimen, so that a substantially monochromatic first light beam is emitted towards the specimen. Providing the first light beam according to this method may render expensive laser devices superfluous, while a substantially monochromatic light beam is provided for illumination of the specimen.

The first light beam may comprise light having spectral components at more than a single wavelength. Such a first light beam may be provided by a laser source, which is capable of simultaneously generating light comprising components of at least two different wavelengths. Alternatively, a "multi-wavelength" first light beam may be produced by a broad-banded light source combined with

a number of optical components inserted in the optical path between the source and the specimen. This last solution may, however, be too complex for practical use.

In a preferred embodiment of the invention, the first light beam is generated by a 488 nm argon-ion gas laser. The target objects in the specimen are, further, stained with at least one fluorescent marker to differentiate them from the objects of the main substance. The specimen is, preferably, provided dispersed on a disc surface having a diameter of, approximately, 120 mm. The laser beam is focused into a circular spot on the specimen during the scanning. The spot diameter is, preferably, between 20-150 μm, more preferably between 20-80 μm and even more preferably between 30-60 μm. Preferably, the spot diameter is adapted to a particular application so that an optimum signal to noise ratio is provided in the detector signal, thereby enhancing the discrimination between target objects and false positive signals. These false positive signals may originate from random noise in the detector and its associated electronic circuitry, or may originate from autofluorescent objects and particles, which may contaminate the specimen.

It may often be desirable to utilise the largest possible spot diameter in the present apparatus, in order to minimise the scan time of the specimen. Several limitations may, however, restrict the possible spot diameter for a particular application. One limitation, in applications involving the detection of fluorescent target objects, may be that a large spot area also tends to illuminate a large number of fluorescent contaminated objects and particles. These objects and particles may provide emitted light of intensity larger than the

intensity provided by an illuminated target object, thereby deteriorating the discrimination between target objects and other objects of the specimen or even completely preventing the detection of a target object.

The maximum light power available from the light source may provide another limitation to the maximum spot size that can be used. However, in a preferred embodiment of the present apparatus, which utilises a laser light source, this potential limitation has not yet been of serious concern.

Thus, an apparatus according to the present invention may be adapted to identify several types of objects, in a variety of applications, with optimum speed and reliability.

Fluorescent light may be emitted from the target objects during scanning when the first light beam irradiates the target objects and their surroundings. The resultant light, produced by the interaction between the objects of the specimen and the first light beam, may comprise an emitted fluorescent light component from the target objects and a component originating from the first light beam. The resultant light may either be transmitted through the disc surface, reflected from the disc surface, or simultaneously reflected and transmitted. Accordingly, the resultant light may be detected either above the disc surface or below the disc surface when the disc is provided in a transparent material.

The detector is naturally selected so that it is sensitive to a difference in a property between the target objects and objects of the main substance, this

property difference being of morphological, magnetic, optical, etc. character.

In an embodiment of the invention where the specimen is scanned by a light source, a light sensitive detector may, obviously, be selected. Several types of devices may be utilised such as CCD devices, photo-transistors, photo-multipliers, etc. depending upon the requirements of a particular application.

In a preferred embodiment of the invention, a photo-multiplier is used as a light detector. This type of detector may produce an electrical output signal substantially proportional to the light intensity striking it. The detector electrical signal may, further, be provided to storage means adapted to store the signal together with one or several corresponding position signals provided by scanning control means, which additionally may be comprised in the present apparatus.

Means may, further, be provided for sampling and digitising at least one electrical signal from at least one detector, such as a photo-multiplier and the corresponding position signals provided by the scanning control means. Accordingly, each time an object is detected, a corresponding coherent data set may be stored in the storage means, and each of the coherent data sets may be seen as representing a unique signal "event".

The coherent data set may thus comprise a number of digitised signals, the number depending upon the utilised number of detectors and the number of signals provided by the scanning control means. Accordingly, each of these signals is, preferably, represented by a series of

digital samples provided by one or several A/D-converters.

By this, each unique "event" detected during the scanning of the specimen, and which may or may not originate from a target object, may be represented by a stored coherent data set. "Events" not originating from target objects may originate from random noise in the detector and its associated electronic circuitry, or may originate from autofluorescent objects and particles that may have contaminated the specimen. These last mentioned "events" are denoted false positive signals in the following.

In a preferred embodiment of the invention, a substantially rectangular slit formed in a (non-transparent) mask inserted in the optical path from the specimen to the photo-multiplier is provided, so that the photo-multiplier "sees" the irradiated part of the specimen through a rectangular aperture. The slit or aperture may be placed with its longest side (the length) in parallel with a radius of the circular solid support holding the specimen.

The dimensions of the aperture are, preferably, adapted to the dimensions of the target objects to be located, in such a manner that the width of the aperture is approximately equal to the dimensions of the target objects and the length is approximately equal to 3-5 times these dimensions, as projected on the specimen. As projected meaning that the dimensions of the aperture should be adapted to any magnification/demagnification provided in the optical path between the specimen and the aperture.

Further, the laser spot irradiating the specimen is, preferably, provided with a diameter approximately equal to the aperture length.

For example, in an embodiment of the invention where the target objects have dimensions of approximately 10 μm, an aperture length of 30-50 μm and an aperture width of 7.5-15 μm may be selected.

One advantage of the aperture is that e.g. fluorescent target objects "appearing" within the aperture boundaries at the detector, irradiated by the first light beam, will provide maximum signal strength from the detector only during that short instant in time where the target object is fully within the boundaries of the aperture. Thereby a very accurate value for the angular co-ordinate of the detected object may be provided.

Another advantage is that the aperture may enhance the discrimination between target objects and objects generating false positive signals based on a size difference between these object groups. A "large" object, i.e. having dimensions larger than the aperture width, and thereby can not belong to the group of target objects may erroneously have been stained with a fluorescent marker and will thus emit light when irradiated by the first light beam. However, such an object will provide maximum signal strength from the detector during a longer time interval than the target objects, due to a longer time of appearance within the boundaries of the aperture. This difference in signal length, as provided by the detector, originating from the size difference between detected objects of the different groups, may be used as a basis for discrimination between target objects and

other objects in the specimen, and thus enhance the detection of target objects.

Further, the specimen may be scanned, along a radius of the disc holding the specimen, by advancing the position of the aperture and the position of the light spot relative to the specimen with equally large steps i.e. tracking each other. Preferably, the steps have a size of 0.5-1.5 times the dimensions of the target objects.

By scanning the first light beam across the specimen according to this method, a pattern of partially overlapping concentric circular curves is produced on the specimen. The overlap of the scan curves will make a particular target objects "appear" at least 2-3 times at the photo-multiplier at a constant rectangular co-ordinate, but at different radial co-ordinates of the aperture. Thereby 2-3 corresponding coherent data sets may be obtained, each set corresponding to electrical signals from the photo-multiplier and the scanning control means.

Signal processing means may subsequently retrieve and use these coherent data sets to enhance the discrimination between signals originating from target objects and false positive signals. This discrimination may be achieved by analysis of correlation between data sets originating at identical angular co-ordinates but at adjacent radial co-ordinates of the aperture.

When the rectangular aperture is used, an elliptical light spot shape on the specimen may, preferably, cover the entire length of the aperture. The elliptical spot shape may be advantageous since it provides a larger

light power within the aperture boundaries than a circular spot, for a fixed light power radiated by the source.

The detection of target objects may be enhanced by inserting one or several optical filters in the light path between the specimen and the detector to attenuate the source light component of the resultant light before it is transmitted to the detector. Preferably, at least one optical filter, preferably a dichroic filter, is inserted in this light path.

The target objects may be stained with different types of fluorescent markers. Preferred marker(s) may be selected according to their optimum excitation light wavelengths and/or their quantum efficiencies. Since, usually, only a particular part of the light spectrum is useful for excitation of a particular type of fluorescent marker, a light source capable of providing light of a sufficiently high intensity relatively close to the optimum excitation wavelength of the marker should be selected.

Further, the target objects may be stained with two or more different fluorescent markers so that the target objects may provide emitted light at several wavelengths when they are irradiated by source light of appropriate spectral distribution. This distribution may be provided by the light source, so that it only provides substantial light intensity at wavelengths located close to an excitation wavelength of a marker.

When the target objects are stained with two or more fluorescent markers, target objects in the specimen may be detected by performing successive scans of the

specimen, a method hereby denoted "multiple pass scan". The light wavelength of the source may be, during each scan, adapted to excite a particular marker on the objects. The bandwidth of optical filters inserted in the light path between the specimen and the detector may also be adapted to transmit only the wavelength range emitted by the particular fluorescent marker currently being excited by the source light during the scanning.

Alternatively, target objects may be detected in a "single pass scan" of the specimen even though the target objects are provided with e.g. two different markers. This may be achieved by simultaneously exciting both markers with a substantially monochromatic light beam, if the optimum excitation wavelengths of the markers are located sufficiently close in the light spectrum. Light emitted from the target objects may then comprise a light component from each of the markers, and the component originating from each marker may be detected by a separate detector provided for each of the markers. At least one optical filter may be inserted in each optical path from the specimen to the detector. Each filter being adapted to transmit to the detector only light emitted from a particular marker.

Utilising several markers may be advantageous to locate a particular type of target objects possessing several characteristics, and where each characteristic of the target object makes it capable of binding a particular type of marker. This type of target objects may be located by, during a first scan of the specimen, locate a first group of objects, which have been stained with a first type of marker, and subsequently during a second scan locate a second group of objects that have been

stained with a second type of marker. By determining the intersection of the two groups, the target objects may be located. Of course, more than two types of markers may be utilised for staining the target objects depending on the particular application and on the number of characteristics of the target objects that have the ability to bind a particular marker.

An area of application, illustrating the importance of the binding of different markers to different object characteristics, is provided in the medical field where detection and analysis of fetal cells from maternal blood provides a very low risk invasive alternative to prenatal diagnostic procedures, such as amniocentesis of chorionic villus sampling. To provide this analysis, at least one fetal cell with a nucleus must be located in a specimen. The specimen may, further, comprise both maternal cells and fetal cells, and both types may be present with or without a cell nucleus. The detection and location of fetal cells with cell nucleuses may be accomplished by utilising a first fluorescent marker conjugated to a probe, such as an oligonucleotide, which is in situ hybridized to mRNA for gamma globin at least at a part of the fetal cells, and utilise a second fluorescent marker, preferably, DAPI or PI that binds to all cell nucleuses.

By scanning the specimen a first time to locate cells stained with the first fluorescent marker and thus belonging to a first group, and a second time to locate cells stained with the second fluorescent marker, the intersection of the cells groups will contain the target cell(s), i.e. fetal cells that also have a nucleus.

Utilising at least two different markers may also be advantageous to enhance the discrimination between false positive signals and signals originating from target objects during or after the scanning of a specimen. The discrimination may be enhanced in a "multiple pass scan" where the specimen may be scanned in a first pass with light adapted to excite a first marker. Coherent data sets obtained during the scanning, which may correspond to detected objects are stored in the memory. Subsequently the specimen may be scanned a second time with light adapted to excite a second marker and the coherent data sets associated with the detected objects may also be stored in the memory. The discrimination may subsequently be provided by comparing signal values from the detector, obtained at identical angular and radial co-ordinates on the specimen, in the two data sets. One criteria for accepting a detector signal as originating from a target object may be that only signals values, in both data sets, larger than a predetermined threshold value are accepted as originating from a target object. Accordingly, signal values above the threshold in only one of the two data sets may be discarded as originating from noise, autofluorescent particles, etc. and thus being false positive. Identical criteria may, naturally, also be used for discrimination between false positive and "true" detector signals as obtained during a "single pass scan" of the specimen.

A fluorescent marker should, preferably, posses a large quantum efficiency at one hand, and at the other hand posses a large difference between the optimum wavelength of excitation light and the optimum wavelength of emission light.

Preferably, Fluorescein or Fluorescein derivatives may be used as a fluorescent marker(s), since these substances are well known, readily available and possess large quantum efficiencies. Further, optimum wavelengths for excitation light and for emission light are located at 505 nm and 516 nm, respectively, for Fluorescein, which makes it possible to excite this substance by a preferred light source, a 488 nm argon-ion gas laser.

The storage means may be located in a personal computer (PC), which is operationally connected with the apparatus of the present invention. The storage means may comprise magnetic, optic or electric storage media, such as hard disc drives, DAT-tapes, floppy discs, CD-ROM discs, EEPROMs, etc. which may be utilised for non-volatile storage of the coherent data sets obtained from the scanning of the specimen(s). The storage means may also comprise intermediate volatile storage means, preferably RAM, to store data sets during the scanning. This may be advantageous in applications where the data rate provided by the A/D converter(s) is/are higher than the maximum storage rate accommodated by the non-volatile memory device.

The storage means may, alternatively, be provided inside the frame of the apparatus in one embodiment of the present invention, thereby providing a convenient portable "stand alone" apparatus.

It some situations, it may be desirable to identify detected target objects after a specimen has been scanned. This may be accomplished, according to a preferred embodiment of the invention, wherein the coherent data sets, corresponding to detected target

objects, may be retrieved from the memory location. Since these coherent data sets contain information related to the position on the specimen (i.e. may be angular and radial co-ordinates) of the selected target objects, the scanning control means may be adapted to place an automated microscope at the position of one particular target object. Thereby, a medical doctor or a laboratory technician may be allowed to perform a detailed examination of the target object to e.g. establish its identity.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 shows an embodiment of an apparatus according to the invention including components provided in an optical path.

DETAILED DESCRIPTION OF A PREFERRED EMBODIMENT

Fig. 1 shows a preferred embodiment of an apparatus according to the invention, adapted to scan large a specimen 14. A member 17 positioned on a frame (not shown) may hold a substantially circular disc 13 with a diameter of 120 mm, the disc providing a specimen 14, which is submitted for scanning.

The specimen may comprise material originating from a blood or tissue sample from a pregnant woman. The specimen may comprise both adult cells and fetal cells, which may be analysed as a part of a prenatal diagnostic procedure. Accordingly, in the present embodiment of the invention, it is highly desirable to detect and determine positions of fetal cells and in particular fetal cells having a cell nucleus so that an analysis of the

chromosomes in the cell nucleus may be provided. Accordingly, target cells in the present application are those fetal cells that comprise a cell nucleus.

However, it is today believed in the medical community that these fetal cells may have a density as small as 1E-9 - 1E-5 in the specimen, and they may be present in as little as 50 % of the population of pregnant women. This very low density makes it necessary to perform a rapid scanning of the specimen if the fetal cells are to be located in a reasonable amount of time.

In order to locate the fetal target cells in the specimen, they are, preferably, stained with Fluorescein or Fluorescein derivative markers.

Preferably, a coherent first light beam 12, from a 488 nm argon-ion gas laser (not shown) is emitted towards the specimen 14 creating an approximately 40 μm diameter laser spot on the specimen 14. The specimen 14 is scanned by this laser spot along a non-linear curve under the control of scanning means 18 comprising DC motor (not shown) and scanning control means (not shown).

The DC motor, which may be directly connected to the member 17 holding the disc 13 through spindle 19, provides a drive mechanism that enables the disc 13 to be rotated about an axis on the frame. The DC motor further comprises an angle encoder (not shown) capable of providing a signal related to the current angular co-ordinate of the member 17 and the disc 13 to the scanning control means. The angular resolution of the angle encoder is, preferably,

$$\theta_0 = \frac{360}{20000} = 0.018 \text{ Degrees.}$$

The rotational speed of the disc 13 is, preferably, adjusted to be within the interval from 200 to 1500 rpm. The scanning control means may comprise servo means adapted control the rpm of the disc, to produce a substantially constant linear velocity of the laser spot on the disc surface, a principle well known from CD players.

Deflecting means, which form part of the scanning means, and comprise a stepper motor (not shown), are further provided so the disc 13 with the specimen 14 may be displaced along a radius of the disc and its circular movement. Thereby providing a scan of the entire surface area of the disc 13 with the specimen 14 by the laser spot. When the deflecting means moves the disc 13 with the specimen along the radius, a non-linear curve comprising a number of concentric partly overlapping circular curves is formed on the disc 13 surface by the laser spot.

The optical system of the apparatus comprises a 488 nm argon-ion gas laser (not shown) used as a light source. The first light beam 12 emitted from the laser is transmitted through a focusing lens 10 and a dichroic filter 9 to a dichroic beam-splitter 6. This beam-splitter 6 serves two purposes, first to reflect the first light beam 12 towards the specimen 14, and second to filter and direct resultant light 15 emitted from the specimen 14 towards a photo-multiplier 1. The resultant light 15 may comprise a light component originating from a reflected portion of the first light beam 12 and a

fluorescent light component emitted from fluorescent target objets (not shown) contained in the specimen 14. The dichroic beam-splitter 6 and the dichroic filter 4 both contribute to attenuate the light component originating from the laser source (not shown), thereby enhancing the signal to noise ratio of light transmitted to the photo-multiplier 1. The resultant light 15 passing dichroic filter 4 is transmitted through a rectangular slit 16 provided in a mask 3 inserted in the optical path to the photo-multiplier 1. The slit 16 is, preferably, provided with dimensions that result in projected dimensions of length 30 μm and width 15 μm, respectively on the photo-multiplier 1. Accordingly, the slit 16 creates a light path aperture of dimensions, which combined with magnification lens 11, defines the dimensions of the irradiated part of the specimen as "seen" by the photo-multiplier i.e. the dimensions of the irradiated specimen area projected upon the photo-multiplier 1.

CLAIMS

1. An apparatus for detecting a property of an object contained in a specimen, comprising

a frame,

a member positioned on the frame and having a surface that is adapted to receive and hold the specimen,

a detector for detection of the property of the object, and

scanning means for scanning the specimen in relation to the detector along a non-linear curve.

2. An apparatus according to claim 1, wherein the member is positioned for rotation about an axis on the frame and the scanning means comprise means for rotating the member about the axis.

3. An apparatus according to claim 1 or 2, further comprising scanning control means for controlling the scanning means for scanning the specimen along a predetermined curve.

4. An apparatus according to claim 3, wherein the scanning control means are adapted to control the scanning means in such a way that the predetermined curve is a substantially circular curve.

5. An apparatus according to claim 3 or 4, further comprising storage means for storage of signals provided

by the detector and corresponding position signals provided by the scanning control means.

6. An apparatus according to claim 5, further comprising means for sampling and digitising the detector signals and the position signals.

7. An apparatus according to any of the preceding claims, further comprising signal processing means connected to the detector and adapted to receive detector signals and detect presence of an object based on the detector signals.

8. An apparatus according to claim 7, wherein position signals relating to detected objects are stored in the storage means.

9. An apparatus according to claim 8, wherein the stored positions of the detected objects are retrieved, and used by said scanning means to position a means for optical inspection of detected objects.

10. An apparatus according to any of the preceding claims, wherein the specimen has an area larger than 500 mm^2.

11. An apparatus according to any of the preceding claims, wherein the specimen has an area larger than 8000 mm^2.

12. An apparatus according to any of the preceding claims, wherein the detector comprises magnetic detection means.

13. An apparatus according to claim 12, wherein the detector comprises a magnetic reading head.

14. An apparatus according to any of the preceding claims, further comprising

a light source for emission of a first light beam towards the specimen held by the member, and wherein

the detector comprises an optical detector for detection of light emitted from the object upon interaction with the first light beam during scanning of the specimen.

15. An apparatus according to claim 14, wherein the scanning means further comprise deflecting means for scanning the first light beam across the specimen along a radius of the circular movement of the member.

16. An apparatus according to claim 14, wherein the light source is positioned for rotation about an axis on the frame and the scanning means comprise means for rotating the light source about the axis.

17. An apparatus according to claim 14, wherein the scanning means further comprise deflecting means for scanning the first light beam across the specimen along a radius of the circular movement of the light source.

18. An apparatus according to claim 14, wherein the scanning means further comprise movable deflecting means for variable deflection of the first light beam.

19. An apparatus according to claim 18, wherein the movable deflecting means comprise a first mirror that is

rotatable around a first axis so that the first light beam can be scanned across the specimen along a substantially circular curve.

20. An apparatus according to claim 19, wherein the first mirror is further rotatable around a second axis for variation of the radius of the circular curve.

21. An apparatus according to any of claims 14-20, wherein a mask is inserted in the optical path between the specimen and the detector, and

the mask comprises at least one transparent aperture.

22. An apparatus according to claim 21, wherein the aperture shape is a substantially rectangular shape.

23. An apparatus according to claims 21 or 22, wherein at least one dimension of the aperture, as projected on the specimen, is between 0.75 and 2 times the dimensions of objects to be detected.

24. An apparatus according to any of claims 14-23, wherein the objects of the specimen are stained with a fluorescent marker.

25. An apparatus according to claim 24, wherein the fluorescent marker is Fluorescein.

26. An apparatus according to any of claims 14-25, wherein the light source is a coherent light source.

27. A method of detecting a property of an object contained in a specimen, comprising the steps of

positioning the specimen on a member having a surface that is adapted to receive and hold the specimen,

scanning the specimen in relation to the detector along a non-linear curve, and

detecting the property of the object during scanning of the specimen.

28. A method according to claim 27, further comprising the step of rotating the member holding the specimen about an axis.

29. A method according to claim 27 or 28, further comprising the step of storing signals relating to the detected property and corresponding data relating to the current position of the member.

30. A method according to claim 29, further comprising the step of sampling and digitising the signals and the data.

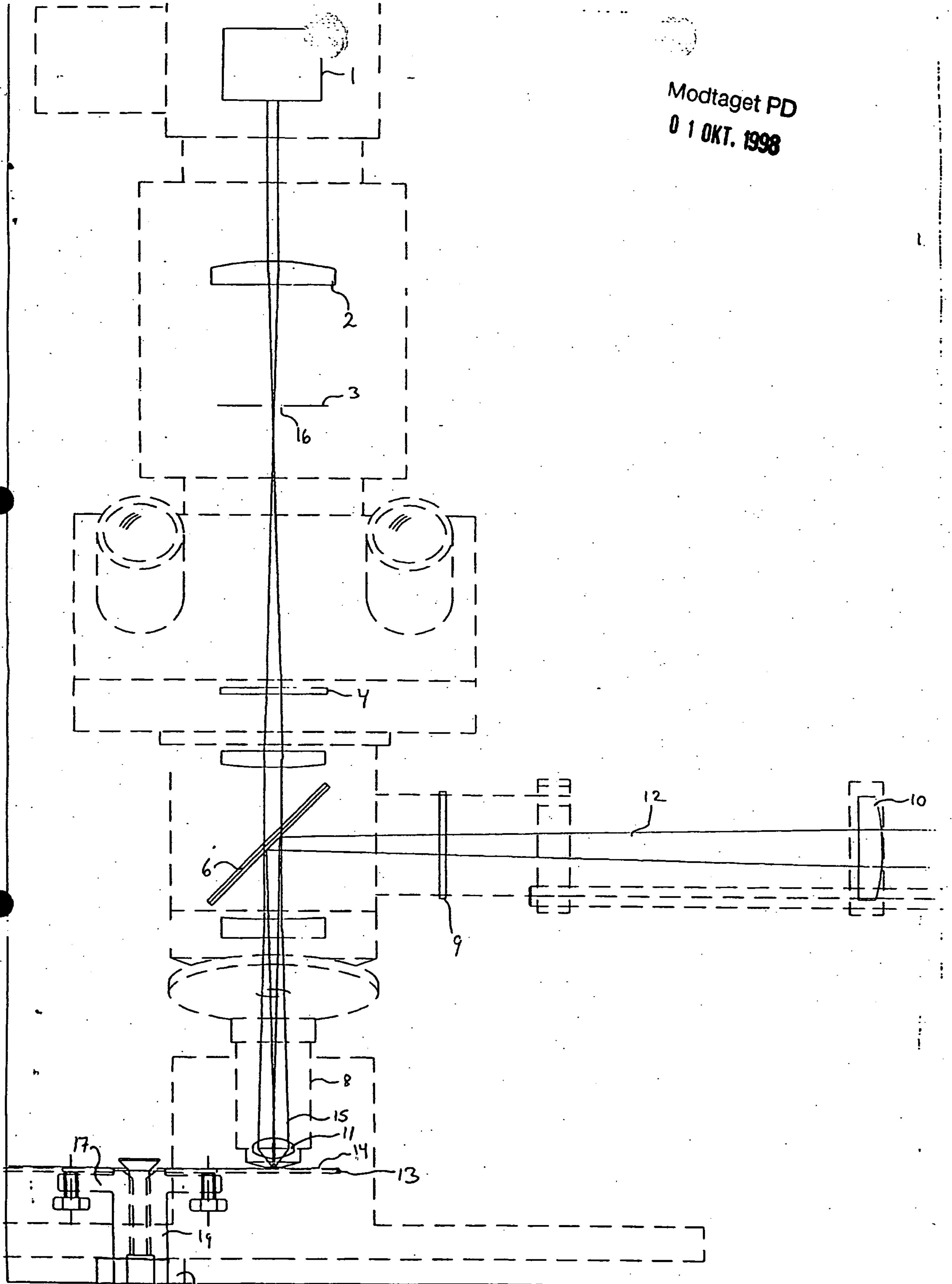

Fig. 1